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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,298	02/08/2000	JUNKO YAMAMOTO	1422-411P	1749
2292	7590	10/05/2005	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH			KIM, YOUNG J	
PO BOX 747			ART UNIT	
FALLS CHURCH, VA 22040-0747			PAPER NUMBER	

1637

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/485,298

Applicant(s)

YAMAMOTO ET AL.

Examiner

Young J. Kim

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20,21,23,24,26-28,30,34,37,43-46,48 and 49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 20,21,23,24,26-28,30 and 44-46 is/are allowed.
- 6) ☒ Claim(s) 34,37,43,48 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This Office Action is responsive to the Amendment received on July 20, 2005.

Preliminary Remark

Claims 1-19, 22, 25, 29, 31-33, 35, 36, 38-42, and 47 have been canceled.

Claim 49 has been added.

Claim Objections

The objection to claims 40 and 42 for depending on a subsequent claim, made in the Office Action mailed on April 20, 2005, is withdrawn in view of the Amendment received on July 20, 2005, canceling the claims.

Claim Rejections - 35 USC § 102

The rejection of claims 31 and 47 under Tibbets et al. (U.S. Patent No. 5,365,455, issued November 15, 1994), made in the Office Action mailed on April 20, 2005 is withdrawn in view of the Amendment received on July 20, 2005, canceling the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 20, 21, 31, 40, 42, 44, and 47 under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993), in view of Kaiser et al. (U.S. Patent No. 5,843,669, issued December 1, 1998, filed November 29, 1996), made in the Office Action mailed on April 20, 2005 is withdrawn in view of a careful reconsideration of the application and Applicants' arguments presented in the Amendment received on July 20, 2005. With regard to claims 31, 40, 42, and 47, the rejection is withdrawn by way of their cancellation.

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The rejection of claims 23, 24, 26, 27, 28, 30, 45, and 46 under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993) in view of Kaiser et al. (U.S. Patent No. 5,843,669, issued December 1, 1998, filed November 29, 1996) and in light of Fuller (U.S. Patent No. 5,432,065, issued July 11, 1995), made in the Office Action mailed on April 20, 2005 is withdrawn in view of a careful reconsideration of the application and Applicants' arguments presented in the Amendment received on July 20, 2005.

The rejection of claims 41 and 43 under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993) in view of Kaiser et al. (U.S. Patent No. 5,843,669, issued December 1, 1998, filed November 29, 1996) and Keller (U.S. Patent No. 5,356,796, issued October 18, 1994) made in the Office Action mailed on April 20, 2005 is withdrawn in view a careful reconsideration of the application and in view of the Amendment received on July 20, 2005.

The rejection of claim 41 has been withdrawn in view its cancellation.

Rejections - Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 34, 37, 43, and 48 under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993) in view of Kaiser et al. (U.S.

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Patent No. 5,843,669, issued December 1, 1998, filed November 29, 1996) and in light of Fuller (U.S. Patent No. 5,432,065, issued July 11, 1995), made in the Office Action mailed on April 20, 2005 is maintained for the reasons of record.

Applicants' arguments presented in the Amendment received on July 20, 2005 have been fully considered but they are not found persuasive.

The present rejection includes new claim 49, in the instant rejection being necessitated by Amendment by its addition to a base claim whose rejection is maintained herein.

Bunn et al. disclose a method of RT-PCR, wherein the method involves the step of reverse transcribing an mRNA template into a cDNA, followed by the amplification (via PCR) of the cDNA (column 7, lines 19-28).

Bunn et al. do not explicitly teach a kit for employing a compound that lowers T_m (melting temperature) value of a double-stranded nucleic acid, wherein said compound is selected from the group consisting of formamide, dimethyl sulfoxide, and trimethyl glycine.

Kaiser et al. disclose a method of amplifying (via PCR) employing 7-Deaza-dATP and 7-Deaza-dGTP (column 24, lines 29-26; column 183, lines 1-9).

Fuller discloses a method of amplifying a nucleic acid (column 1, line 46), wherein said method involves the use of 7-deaza nucleotide, specifically 7-deaza-dGTP (column 7, line 15), in a solution containing formamide (column 7, lines 20-21).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to package the ingredients of Bunn et al. and Kaiser et al. and Fuller et al. into a kit in arriving at the claimed invention for the following reasons.

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The technique of RT-PCR is a well-known process of amplifying a sample in a species, wherein the target nucleic acid to be amplified is an RNA or mRNA, as evidenced by Bunn et al.

While Bunn et al., in their process of reverse-transcriptase mediated synthesis of cDNA and their subsequent amplification, involves dNTP and not their analogs as claimed, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the dNTP nucleotide analogs of Kaiser et al. for the advantage provided their use, the advantage of which had been explicitly disclosed by Kaiser et al.:

“The 7-deaza purine analogs (7-deaza-dATP and 7-deaza-dGTP) serve to destabilize regions of secondary structure by weakening the intrastrand stacking of multiple adjacent purines. This effect can allow amplification of nucleic acids that, with the use of natural dNTPs, are resistant to amplification because of strong secondary structure” (column 183, lines 1-8).

Hence, one of ordinary skill in the art at the time the invention was made would have been motivated to package the reagents involved in the amplification reaction of Bunn et al. with the 7-deza nucleotide analogs of Kaiser et al, because by doing so, one of ordinary skill in the art would have been able to amplify target nucleic acids having a strong secondary structure.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at such combination as the incorporation of nucleotide analogs during primer extension as already been demonstrated to be feasible by Kaiser et al.

With regard to the inclusion of a compound that lowers the melting temperature of a double-stranded nucleic acids in the same kit, wherein said compound is a formamide, such

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inclusion would have also been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made based on the explicit teaching of Fuller:

“This invention provides an alternative to these procedures, and involves use of a denaturing reagents which decreases the melting temperature of the DNA. Some DNA denaturing reagents e.g., urea and formamide, do decrease the melting temperature of DNA by about 0.5°C for each 1% (vol/vol) concentration” (column 3, lines 3-5, Fuller).

It is well known that for an amplification reaction to occur, the amplification primers must hybridize to single-stranded nucleic acid templates. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the reagents that preclude template double-strand formation, via use of 7-deaza nucleotide analogs as well as formamide and package these ingredients into the same kit.

As Fuller demonstrates that amplification with solution containing formamide and at least one 7-deaza nucleotide analog (specifically, 7-deaza-dGTP) has been feasible, one of ordinary skill in the art would have had no doubt that addition of an additional 7-deaza nucleotide analog as that of Kaiser et al. would have worked equally well, giving said ordinarily skilled artisan a clear motivation at packaging the ingredients together in a same kit in view of the conventionality of kits in the analytical arts for the advantages of convenience, cost-effectiveness, matched and/or preweighed components, etc.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Response to Arguments:

Applicants argue that while Bunn ('961 patent) disclose a method of RT-PCR and Kaiser ('669 patent) disclose a method of PCR employing 7-Deaza-dATP and 7-Deaza-dGTP, none of

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the artisans teach the use of claimed nucleotide analogs during the reverse transcription steps nor point out any motivation in generating a cDNA (via reverse transcription) containing the claimed nucleotide analogs.

While the above argument is found persuasive for the method claims, claims drawn to a kit comprising the reagents of the cited references are deemed obvious for the following reasons.

A kit comprising the claimed ingredients need not be packaged together for the same reason as the reasons set forth in the application, as the kit *for* doing a particular method is only an intended use limitation. So long as a motivation to package the same ingredients of the claimed kit, whether it be the same motivation or not, the claimed kit would be obvious.

The issue at hand is whether there exists a *prima facie* motivation for one of ordinary skill in the art at the time the invention was made to derive a kit comprising the claimed nucleotides and a compound for lower the T_m value of a double-stranded nucleic acid.

It is clear that the artisans disclose the use of 7-Deaza-dATP and 7-Deaza-dGTP for the explicit benefit of, “destabilize[ing] regions of secondary structure by weakening the intrastrand stacking of multiple adjacent purines... allow[ing] amplification of nucleic acids that, with the use of natural dNTPs, are resistant to amplification because of strong secondary structure” (column 183, lines 1-8; Kaiser et al.).

Further, the use of formamide for the same motivation is also disclosed by the cited artisans:

“This invention provides an alternative to these procedures, and involves use of a denaturing reagents which decreases the melting temperature of the DNA. Some DNA

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denaturing reagents e.g., urea and formamide, do decrease the melting temperature of DNA by about 0.5°C for each 1% (vol/vol) concentration” (column 3, lines 3-5, Fuller).

Again, it is well known that for an amplification reaction to successfully occur, the amplification primers must hybridize to single-stranded nucleic acid templates. Therefore, one of ordinary skill in the art at the time the invention was made would had a *prima facie* motivation for combining the reagents that preclude template double-strand formation (*i.e.*, *hair pin*), via use of 7-deaza nucleotide analogs as well as formamide and package these ingredients into the same kit.

MPEP 2144.06, also supports such rationale in combining art recognized equivalence for the same purpose (*citing In re Kerkhoven*):

“It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior-art.” *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

With regard to claim 49, the use of thermostable polymerase for PCR is well-known in the art and would have been obvious to include in the claimed kit. Also, column 7, line 68 of Bunn et al. evidences the use of Taq polymerase (a thermostable polymerase).

Therefore the invention as claimed is *prima facie* obvious and the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Inquiries

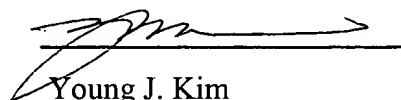
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official

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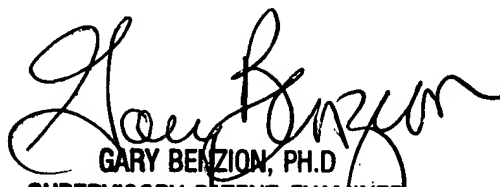
Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.



Young J. Kim
Patent Examiner
Art Unit 1637
10/3/2005

**YOUNG J. KIM
PATENT EXAMINER**

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